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A Wittig Type Rearrangement of 2-Methoxycarbonyl-2-phenyl-1,3-dithiane and 2,2-Diphenyl-1,3-dithiepane

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The lithiations of 2-methoxycarbonyl-2-phenyl-1,3-dithiane and 2,2-diphenyl-1,3-dithiepane with an excess of lithium diisopropylamide occurred at C–4 in the respective rings, followed by a Wittig type rearrangement to give the corresponding thiolate anions which afforded 3-alkylthio-2-methoxycarbonyl-2-phenyltetrahydrothiophenes and 3-alkylthio-2,2-diphenyltetrahydrothiopyrans, respectively, on trapping with alkyl halides.

KEY WORDS: Wittig rearrangement/ 2-Methoxycarbonyl-2-phenyl-1,3-dithiane/ 2,2-Diphenyl-1,3-dithiepane/

Recently, we have found[1] that 2,2-disubstituted 4-lithio-1,3-dithianes undergo a Wittig type rearrangement to give the anions of 2,2-disubstituted tetrahydrothiophene-3-thiols. This may be the first example illustrating the unstableness of a certain of 4-lithio-1,3-dithianes in contrast with the stableness of 2- and 4-lithio-1,3-dithianes derived from 2-alkyl- and 2-cyclohexylidene-1,3-dithianes, respectively.[2,3] On the other hand, both 2- and 4-lithio-1,3-dithiolanes are extremely unstable.[4,5] The former undergoes facile cycloelimination to form ethylene and dithiocarbonates and the latter gives rise to the versatile thiocarbonyl compounds and ethenethiolate anion *via* another type of cycloelimination. With these backgrounds, we have investigated the behavior of 4-lithio derivatives (**2** and **6**) of 2-methoxycarbonyl-2-phenyl-1,3-dithiane (**1**) and 2,2-diphenyl-1,3-dithiepane (**5**) which would be derived from these cyclic 1,3-dithioacetals with lithium diisopopylamide (LDA) at low temperature. These compounds seem to be adequate starting substrates, because the compound **1** possesses a practicability of further structural conversions of its methoxycarbonyl group and the compound **5** is a typical higher homologue of 2,2-disubstituted 1,3-dithianes. Also, these compounds are easily available by condensation of methyl benzoylformate with 1,3-propanedithiol and that of benzophenone with 1,4-butanedithiol, respectively, in the presence of aluminum chloride. The lithiation of **1** with an excess of LDA in tetrahydrofuran proceeded smoothly to afford 4-lithio derivative (**2**) of **1**. However, it was unstable and hence underwent a Wittig type rearrangement to give 2-methoxycarbonyl-2-phenyltetrahydrothiophene-3-thiolate anion (**3**). On trapping with methyl and ethyl iodide, **3** afforded new tetrahydrothiophene derivatives **4a** and **4b**, respectively (Table I). The lithiation of **5** with an excess of LDA in tetrahydrofuran also occurred at C–4 in the ring, and the resulting 4-lithio derivative (**6**) of **5** likewise underwent a Wittig type rearrangement to give the anion of 2,2-diphenyltetrahydrothiopyran-3-thiol (**7**), followed by trapping with alkyl halides leading to the formation of a variety of 3-alkylthio-2,2-diphenyltetrahydrothiopyrans (**8**) in excellent yields. Also, the intermediate anionic species **7** was

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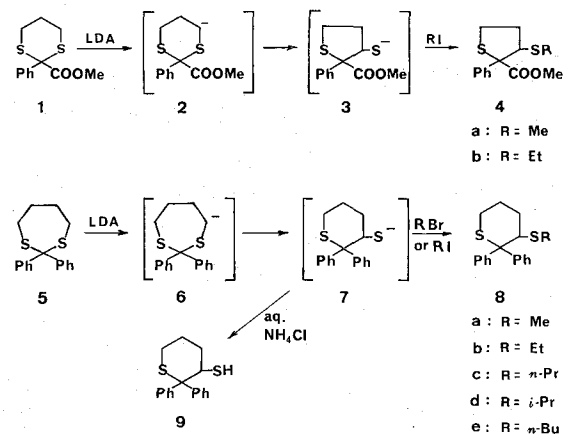

converted to 2,2-diphenyltetrahydrothiopyran-3-thiol (**9**) by trapping with a saturated aqueous solution of ammonium chloride (Table I).

The conversion of **2** into **3** or that of **6** into **7** can be accounted for by a ionic mechanism involving a 1,2-shift of C-2 from S-3 to C-4 carbanion accompanied by the simultaneous S-3 thiolate expulsion.[1] However, it can also be explained by a radical mechanism[6] involving an intramolecular recombination of an ion-biradical which would be formed *via* a homolytic cleavage between C-2 and S-3 and the subsequent charge transfer of C-4 to S-3. No correct explanation has been given yet concerning the Wittig type rearrangement. Table II give ^{1}H-NMR spectral and analytical data of the obtained products. The compuunds **4a** and **4b** possess two dissimilar asymmetric centers, and hence four stereoisomers are possible. Each of

Table I. The Wittig Type Rearrangement of 2-Methoxycarbonyl-2-phenyl-1,3-dithiane (**1**) and 2,2-Diphenyl-1,3-dithiepane (**5**)

Entry	Starting substrate	Trapping agent	Reaction temperature/time with trapping agent	Eluent used in chromatography	Product (yield/%)
1	**1**	MeI	25°C/30 min	CH_2Cl_2/hexane (1:1)	**4a** (65)
2	**1**	EtI	25°C/30 min		**4b** (48)
3	**5**	MeI	25°C/30 min	ether/hexane (1:5)	**8a** (95)
4	**5**	EtI	25°C/30 min		**8b** (95)
5	**5**	*n*-PrI	25°C/30 min		**8c** (95)
6	**5**	*i*-PrI	25°C/30 min		**9** (96)[a]
7	**5**	*i*-PrI	25°C/24 h	CH_2Cl_2/hexane (1:7)	**8d** (87)
8	**5**	*i*-PrI	reflux/30 min		**8d** (78)
9	**5**	*n*-BuI	25°C/30 min	ether/hexane (1:5)	**8e** (99)
10	**5**	*n*-BuBr	25°C/24 h	CH_2Cl_2/hexane (1:6)	**8e** (85)
11	**5**	H_2O[b]	25°C/0 min	ether/hexane (1:5)	**9** (100)

a) The obtained product was **9**, suggesting that **7** is unreactive to *i*-PrI under given reaction conditions (25°C/30 min) and hence it was trapped by the saturated aqueous solution of ammonium chloride used in the work-up procedure.
b) Water including ammonium chloride up to saturation.

Table II. ^{1}H-NMR Spectral and Analytical Data of the Obtained Products

Product[a]	^{1}H-NMR (δ, in $CDCl_3$)[b]	Found (Calcd) (%)	
		C	H
4a	1.70 (s, 3H), 1.9–2.6 (m, 2H), 2.7–3.2 (m, 2H), 3.57 (s, 3H), 3.8–4.2 (m, 1H), 6.9–7.5 (m, 5H)	58.00 (58.18)	6.29 (6.01)
4b	1.07 (t, 3H), 1.9–2.6 (m, 4H), 2.7–3.3 (m, 2H), 3.59 (s, 3H), 3.9–4.3 (m, 1H), 7.0–7.6 (m, 5H)	59.63 (59.54)	6.42 (6.42)
8a	1.74 (s, 3H), 1.9–2.6 (m, 6H), 3.6–3.9 (m, 1H), 7.0–7.7 (m, 10H)	71.71 (71.95)	6.76 (6.71)
8b	0.97 (t, 3H), 1.8–2.6 (m, 8H), 3.6–3.9 (m, 1H), 7.0–7.8 (m, 10H)	72.81 (72.56)	7.17 (7.05)
8c	0.4–0.9 (m, 3H), 1.1–1.6 (m, 2H), 1.9–2.7 (m, 8H), 3.6–4.0 (m, 1H), 7.1–7.8 (m, 10H)	73.28 (73.11)	7.28 (7.36)
8d	0.90 (d, 3H), 1.01 (d, 3H), 1.6–2.5 (m, 7H), 3.5–3.8 (m, 1H), 6.9–7.6 (m, 10H)	73.15 (73.11)	7.30 (7.36)
8e	0.6–1.6 (m, 7H), 1.8–2.6 (m, 8H), 3.6–3.9 (m, 1H), 7.0–7.8 (m, 10H)	73.86 (73.63)	7.74 (7.65)
9	1.4–2.6 (m, 7H), 4.2–4.6 (m, 1H), 7.0–7.7 (m, 10H)	71.33 (71.28)	6.40 (6.33)

a) The melting points of **8a** and **9** are 105–107°C (from hexane) and 118–119°C (from hexane), respectively. All other products are oily substances.
b) Measured at 25°C.

the compounds **8** and **9** is a racemic mixture, and only 2,2-diphenyl-3-methylthiotetrahydrothiopyran (**8a**) and **9** were solid substances, all others were oily substances.

EXPERIMENTAL

The Formation of 2-Methoxycarbonyl-3-methylthio-2-phenyltetrahydrothiophene (4a) and 3-Ethylthio-2-methoxycarbonyl-2-phenyltetrahydrothiophene (4b). A solution of lithium diisopropylamide (LDA), prepared from diisopropylamine (0.35 g, 3.5 mmol) in tetrahydrofuran (7 ml) and 1.56 molar solution (2.12 ml, 3.3 mmol) of butyllithium in hexane, is added to a solution of **1** (0.331 g, 1.3 mmol) in tetrahydrofuran (4 ml) with stirring at −78°C under nitrogen. The reaction mixture is allowed to warm to room temperature and the stirring is continued for 30 min at that temperature. The mixture is cooled again to −78°C, and methyl iodide (0.51 g, 3.6 mmol) or ethyl iodide (0.56 g, 3.6 mmol) is added with stirring. After the addition, the mixture is warmed to room temperature, and stirred an additional 30 min. Then, it is quenched with 20 ml of a saturated aqueous solution of ammonium chloride, and is extracted with ether (3×40 ml). The combined ethereal extracts are dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue, which is subjected to column chromatography on silica gel.

The Formation of 3-Alkylthio-2,2-diphenyltetrahydrothiopyrans (8). The same amount of LDA, prepared similarly as above, is added to a solution of **5** (0.372 g, 1.3 mmol) in tetrahydrofuran (4 ml) with stirring at −78°C under nitrogen. The reaction mixture is processed similarly as above till the addition of alkyl halide. After the addition of an appropriate alkyl halide (3.6 mmol), the reaction mixture is warmed to room temperature, and

stirred an additional 30 min or 24 hr. Only in Entry 8, the reaction mixture is refluxed for 30 min. Then, it is worked up according to the above outlined procedure except that the eluent used in column chromatography is different as shown in Table I.

The Formation of 2,2-Diphenyltetrahydrothiopyran-3-thiol (9). Twenty ml of a saturated aqueous solution of ammonium chloride is added in the place of alkyl halide used in the above experiment. After the usual work-up procedure, the product **9** is separated by column chromatography on silica gel.

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